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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,358	03/09/2001	Robert A. Ach	10971722-2	7724

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/802,358	Applicant(s) Ach
	Examiner Arun Chakrabarti	Art Unit 1634

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Feb 3, 2003*.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *17-20 and 24-44* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *17-20 and 24-44* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). ___
4) [ ] Interview Summary (PTO-413) Paper No(s). ___
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [X] Other: *Detailed Action*

DETAILED ACTION

Specification

1. Applicant's request for reconsideration (a telephone interview with Gary Benzion on May 20, 2003) of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claim Rejections - 35 USC § 112

2. ***The following is a quotation of the first paragraph of 35 U.S.C. 112:***

> ***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

3. Claims 17-20 and 24-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses E. coli and B. subtilis PAP1 and PAP2 which corresponds to the two species of the prokaryotic RNA polymerases. Claims 17-20 and 24-44 are directed to encompass any RNA polymerases from any prokaryotic organism. None of these enzymes meet

the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

The fundamental rule regarding the written description rejection as taught in Lilly and Fiers is that there must be structure associated with functional language. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that, "conception of any chemical substance requires definition of that substance other than by its functional utility." Here the claims are solely functional, drawn only to an enzyme activity, with no structure provided whatsoever.

There is no disclosure not only of the detailed chemical structure of the encompassed enzymatic proteins, but even for any domains or regions required for polyA polymerase activity. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

An applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25

USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Moreover, it is well known in the art that an upstream consensus sequence such as AAUAAA of the gene encoding prokaryotic polyA polymerase is not required for its function, whereas in eukaryotic organisms, the same consensus sequence is required for its function. There is insufficient disclosure in the specification or claim which gene sequence (s) correlate(s) the structure and function, especially the characteristic feature of the claimed invention i.e., end-labeling ribonucleic acids with non-radioactively labeled ribonucleotides using the prokaryotic RNA polymerase.

Non-radioactive labels such as fluorescein, TAMRA and Cy3 etc. are disclosed in the claimed invention. There is no disclosure either in the specification or claim whether all non-radioactive labels such as biotin and avidin would function with the prokaryotic polyA polymerase. Therefore, only E. coli and B. subtilis PAP1 and PAP2 and labels such as fluorescein, TAMRA and Cy3 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 17-20, 24, 25, 26, 28-32, and 36-41 are rejected under 35 U.S.C. 103(a) over Martin et al. (RNA, (1998), Vol. 4, pages 226-230) in view of Cao et al. (Proceedings of the National Academy of Sciences, (USA), (1996), Vol. 93, pages 11580-11585) further in view of Stratagene Catalog (1988, page 39).

Martin et al teach the reagents and methods for end-labeling ribonucleic acids with non-radioactively labeled ribonucleotides comprising:

a non-radioactively labeled ribonucleotide which is directly detectable ; and

an eukaryotic poly(A) polymerase (Abstract and RESULTS and DISCUSSION Section, Labeling of RNA with nonradioactive nucleotides Subsection, and Figures 1-4).

Martin et al teach the reagents and methods, wherein the non-radioactively labeled ribonucleotide is a non-radioactively labeled ATP and UTP analog (Abstract).

Martin et al teach the reagents and methods, wherein the non-radioactively labeled ribonucleotide is fluorescently labeled with fluorophore fluorescein (Abstract and RESULTS and DISCUSSION Section, Labeling of RNA with nonradioactive nucleotides Subsection).

Martin et al do not teach the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase Escherichia coli poly(a) polymerase 1 or 2.

Cao et al. teach the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase Escherichia coli poly(a) polymerase 1 or 2 (Abstract and MATERIALS AND METHODS and Figures 1-5).

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase of Cao et al. into the composition of Martin et al, since Cao et al. state, "The identification of the gene for the second E. Coli. poly(A) polymerase opens the way for the detailed investigation of the metabolic role of mRNA polyadenylation by studying the consequences of disruption of either or both of the poly(A) polymerase genes (Page 11585, Column 2, last sentence)". By employing scientific reasoning, an ordinary artisan would have combined and substituted a functional equivalent poly(A) polymerase of Cao et al. into the composition of Martin et al, in order to improve the detailed investigation of the metabolic role of mRNA polyadenylation. An ordinary practitioner would have been motivated to combine and substitute the reagents and methods, wherein the functional equivalent prokaryotic poly(A) polymerase is a bacterial polymerase of Cao et al. into the composition of

Martin et al, in order to achieve the express advantages , as noted by Cao et al., of an invention which provides the detailed investigation of the metabolic role of mRNA polyadenylation by studying the consequences of disruption of either or both of the poly(A) polymerase genes.

Martin et al. in view of Cao et al. do not teach the motivation to combine all the reagents for end-labeling a ribonucleotide in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, non-radioactively labeled ribonucleotide and a prokaryotic poly(A) polymerase of Martin et al. in view of Cao et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control (page 39, column 1).

6. Claims 27, 34, 35, 42- 44 are rejected under 35 U.S.C. 103(a) over Martin et al. (RNA, (1998), Vol. 4, pages 226-230) in view of Cao et al. (Proceedings of the National Academy of Sciences, (USA), (1996), Vol. 93, pages 11580-11585) further in view of Stratagene Catalog (1988, page 39) further in view of Waggoner et al. (U.S. Patent 6,479,303 B1) (November 12, 2002).

Martin et al. in view of Cao et al. further in view of Stratagene Catalog teach the method of claims 17-20, 24, 25, 26, 28-32, and 36-41 as described above.

Martin et al. in view of Cao et al. further in view of Stratagene Catalog do not teach the method, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7.

Waggoner et al. teach the method, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 (Abstract, Column 11, lines 42-60 and Table 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the reagents and methods, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 of Waggoner et al. into the composition of Martin et al in view of Cao et al. further in view of Stratagene Catalog since Waggoner et al. states, "The development of such multichromophore complexes is particularly useful for multicolor detection systems (Column 11, lines 58-60)". An ordinary practitioner would have been motivated to combine and substitute the reagents and methods, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 of

Waggoner et al. into the composition of Martin et al in view of Cao et al. further in view of Stratagene Catalog in order to achieve the express advantages , as noted by Waggoner et al., of an invention which provides the development of multichromophore complexes particularly useful for multicolor detection systems.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

May 21, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER